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09/636,289	08/10/2000	Volker Landschutze	514413-3834	7068

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EXAMINER	
FOX, DAVID T	

ART UNIT	PAPER NUMBER
1638	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/636,289	Landschutze
Examiner	**Group Art Unit**
Fox	1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE -3- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 2/28/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-29 is/are pending in the application.

Of the above claim(s) 25-28 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-24 and 29 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☑ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been ☑ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3, 6

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

Applicant's election with traverse of Group I in Paper No. 10 is acknowledged. The traversal is on the ground(s) that there would be no burden to search all of the groups since they overlap. This is not found persuasive because the starch of Group II is physiologically distinct from the nucleic acid and transformed hosts of Group I, and can be made by a distinct process from that of Group I, and so are properly restrictable per MPEP 806.05(f), as stated in the last Office action.

The requirement is still deemed proper and is therefore made FINAL.

Claim 29 is objected to for its dependency upon non-elected claim 28.

Claim 19 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should depend upon other claims in the alternative only, and because a multiple dependent claim should not depend upon another multiple dependent claim such as claim 16. See MPEP § 608.01(n). In the interest of compact prosecution, the claim has been treated on the merits. Such treatment does not relieve Applicant of the responsibility to respond to this objection.

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16-18 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for

example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 8-11 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in its recitation of "GBSSI" and "BE" as it is unclear what is intended. Replacement of these terms with --granule-bound starch synthase I (GBSSI)-- and --branching enyzme (BE)--, respectively, in claim 1, would obviate this rejection.

Claim 2, line 2 is indefinite in its recitation of "consisting in the introduction" which is awkward. Replacement of "in" with --of-- would obviate this rejection.

Claims 2-3, 8-11 and 16-18 are indefinite in their recitation of "one or more foreign nucleic acid molecules whose presence and/or expression leads to a decrease in the activity [or inhibition of the expression] of...GBSSI... and... BE proteins" (claims 2-3 and 8-11) or "one or more foreign nucleic acid molecules which encode proteins having the enzymatic activity of GBSSI and BE proteins" (claims 16-18). It is unclear whether a single nucleic acid molecule is intended to cause a decrease in the activity or expression of both GBSSI and BE proteins, or whether a single nucleic acid molecule is intended to encode a protein which has the enzymatic activity of both GBSSI and BE.

Claim 4, line 1 is indefinite in its recitation of "[T]he transgenic plant cells" which lacks antecedent basis in claim 2. Replacement of "cells" with --cell-- would obviate this rejection.

Claim 15 is indefinite in its recitation in line 1 of "[T]he reproductive material" which lacks antecedent basis in claim 12. Deletion of "The" would obviate this rejection.

Claims 16-18 provide for the use of nucleic acid molecules, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 16-17 are indefinite in their recitation of "enzymatic activity of GBSSI and BE" as it is unclear which aspect of enzymatic activity, namely substrate binding, kinetics, catalytic reaction, final product produced, etc. is intended.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of nucleic acid molecules which somehow decrease the activity of GBSSI and BE enzymes without affecting the expression of the genes

encoding them (claims 1-2), or which either simultaneously inhibit the expression of both GBSSI and BE (claim 3 and claim 4, parts a and b) or encode a single protein with the enzymatic activity of both GBSSI and BE or encode a multitude of fragments thereof (claim 16), or a multitude of nucleic acid molecules of any sequence and from any source and of any length which inhibit the expression of either GBSSI or BE from any source, or a multitude of nucleic acid molecules encoding any type of branching enzyme, or a multitude of nucleic acid molecules of any sequence which encode a multitude of ribozymes thereto (claim 4, part c) or which comprise a multitude of *in-vivo*-produced mutants thereof (claim 4, part d); plants transformed therewith, and methods for their use.

In contrast, the specification only provides guidance for constructs comprising at least 1330 base pairs of the potato GBSSI coding sequence and the entire potato BEI coding sequence each in antisense orientation with respect to a plant-expressible promoter, plants transformed therewith, and methods for their use. No guidance is provided for any structural features of any nucleic acid sequences which simultaneously inhibit the expression of both GBSSI and BE, or which simultaneously or individually decrease the activity of either or both enzyme in the absence of affecting the expression of the corresponding gene, or for any structural features of any nucleic acid molecule which comprises a mutant or encodes a ribozyme. Furthermore, no guidance is provided for the structural features of any individual GBSSI or BE gene or the encoded protein from non-plants or from plants other than potato, or for any other type of BE gene other than the

BEI gene. Finally, no guidance is provided for a multitude of fragments of BE or GBSSI genes encoding a multitude of BE or GBSSI protein fragments.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the genus as broadly claimed. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time it was made.

See *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021 and 1027, (Fed. Cir. 1991), where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Claims 1-24 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to nucleic acid constructs comprising at least 1330 base pairs of potato GBSSI gene and the entire coding sequence of the potato BEI gene, each in antisense orientation with respect to a plant-expressible promoter, plants transformed with both constructs, and methods for producing starch with decreased amylose and increased phosphate content comprising potato transformation with said constructs; does not reasonably

provide enablement for claims broadly drawn to the obtention of transformed plants producing said modified starch following transformation with a single nucleic acid molecule which somehow reduces the expression or activity of both GBSSI and BE, a single nucleic acid molecule which encodes a single protein with the enzymatic activity of both GBSSI and BE, nucleic acid molecules from sources other than potato which encode GBSSI and BE, nucleic acid molecules encoding other types of BE besides BEI, nucleic acid molecules encoding a multitude of ribozymes thereto or comprising a multitude of *in-vivo*-produced mutants thereof; or for the obtention of modified starch following the transformation of non-potatoes with either the exemplified or non-exemplified sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a multitude of nucleic acid molecules which somehow decrease the activity of GBSSI and BE enzymes without affecting the expression of the genes encoding them (claims 1-2), or which either simultaneously inhibit the expression of both GBSSI and BE (claim 3 and claim 4, parts a and b) or encode a single protein with the enzymatic activity of both GBSSI and BE or a multitude of fragments thereof (claim 16), or a multitude of nucleic acid molecules of any sequence and from any source and of any length which inhibit the expression of either GBSSI or BE from any source, or a multitude of nucleic acid molecules encoding any type of branching enzyme, or a multitude of nucleic acid molecules of any sequence which encode a multitude of ribozymes thereto (claim 4, part c) or which comprise a multitude of

in-vivo-produced mutants thereof (claim 4, part d); plants transformed therewith, and methods for their use to produce transformed plants of any species which produce a modified starch having increased phophate content and decreased amylose content.

In contrast, the specification only provides guidance for constructs comprising at least 1330 base pairs of the potato GBSSI coding sequence and the entire potato BEI coding sequence each in antisense orientation with respect to a plant-expressible promoter, plants transformed therewith, and methods for their use to produce modified potato starch. No guidance is provided for any structural features of any nucleic acid sequences which simultaneously inhibit the expression of both GBSSI and BE, or which simultaneously or individually decrease the activity of either or both enzyme in the absence of affecting the expression of the corresponding gene, or for any structural features of any nucleic acid molecule which comprises a mutant or encodes a ribozyme. Furthermore, no guidance is provided for the structural features of any individual GBSSI or BE gene or the encoded protein from non-plants or from plants other than potato, or for any other type of BE gene other than the BEI gene. Furthermore, no guidance is provided regarding the obtention of modified starch following the transformation of plants other than potato with the potato or non-potato-derived sequences. Finally, no guidance is provided for a multitude of fragments of BE or GBSSI genes encoding a multitude of BE or GBSSI protein fragments, or for the use of these gene fragments to produce plants with modified starch.

The obtention of modified starch following plant transformation with sequences that inhibit the expression of genes encoding enzymes involved in starch synthesis, such as antisense

RNA-encoding constructs, is unpredictable. Kull et al teach that antisense GBSSI sequences from barley had no effect on the starch produced by potato plants transformed therewith (see, e.g., page 69, Abstract).

The ability of a single nucleic acid molecule, corresponding to a single gene encoding a single protein, to affect the activity or expression of multiple enzymes, is unpredictable and unlikely. Kuipers et al teach that a nucleic acid construct which reduced GBSS expression had no effect on any other enzyme involved in starch metabolism (see, e.g., page 43, Abstract, penultimate sentence).

Furthermore, non-exemplified means of gene inhibition such as ribozymes have not been demonstrated to effect gene inhibition or phenotypic change *in planta*. See Evans et al, page 344S, paragraph bridging columns 1 and 2, who teach that neither cleavage of target RNA nor reduction in the target gene product were observed in plant cells. See also Mazzolini et al, who teach low activity of ribozymes in intact plant cells and negligible reduction of enzyme activity following cell transfection with genes encoding ribozymes specific for the target enzyme, even when the ribozyme genes themselves were highly expressed (see, e.g., page 716, column 1, first full paragraph; page 722, bottom paragraph of each column; page 723, column 1; page 726, bottom paragraph of each column; page 728, column 2, first full paragraph; page 729, first full paragraph of column 1, first paragraph of column 2). Furthermore, Kull et al cited above teach that ribozymes were ineffective in altering starch properties (see, e.g., page 69, Abstract).

In addition, *in vivo* mutagenesis in plants is unpredictable. Hohn et al teach that techniques which were successful in animals had a much lower transformation rate in plants, which presented cellular barriers, and that the expected base pair changes were not obtained (see, e.g., page 8322, column 1 and paragraph bridging the columns). Zhu et al teach that some predicted amino acid changes following *in-vivo* mutagenesis were unpredictably never observed (see, e.g., page 8771, Table 2, second through fourth rows).

Given the unpredictability, claim breadth, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify, develop and obtain a multitude of non-exemplified nucleic acid sequences, from a multitude of sources and encoding a multitude of non-exemplified proteins or ribozymes or mutants; and to evaluate them for their ability to modify the amylose or phosphate content of starch produced by potatoes or a multitude of non-exemplified plants transformed therewith.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-24 are rejected under 35 U.S.C. 102(b) as being anticipated by each of Safford et al and Visser et al.

The claims are broadly drawn to a composition comprising a single nucleic acid which inhibits expression or activity of either GBSSI or BEI, wherein the presence of more than one of

these nucleic acids would inhibit both GBSSI and BEI, and to plant cells and plants transformed with one of the single nucleic acids.

Safford et al teach plant cells and plants transformed with a composition comprising the potato BE gene in antisense orientation with respect to a promoter, wherein BE activity was reduced (see, e.g., page 156, column 2; page 157, column 1; page 159, Figure 1).

Visser et al teach plant cells and plants transformed with a composition comprising the potato GBSSI gene in antisense orientation with respect to a promoter, wherein GBSSI amount and/or activity was reduced (see, e.g., pages 290-291; page 293, column 1, bottom paragraph and Table 3).

Claims 1-6, 8, 10, 12-16, 19-24 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Flipse et al.

The claims are broadly drawn to compositions comprising a single nucleic acid which inhibits expression or activity of either GBSSI or BEI, and transformed plants containing said nucleic acids, wherein said plants produce starch with an amylopectin content of at least 90% and with other modifications, and a method for producing modified starch comprising extracting the starch from said transformed plants.

Flipse et al teach potato plants which contain a mutant GBSSI gene ("*amf*" or "waxy") which results in the inhibition GBSSI activity and inhibition of any amylose production, wherein said plants were transformed with a nucleic acid comprising a potato BEI gene in antisense orientation with respect to a promoter, wherein said transformed plants exhibited inhibited BEI

activity and produced starch which was modified in its structural properties due to an elevated gelatinization temperature (compared to wild-type or waxy mutant plants) and with an amylopectin content of 100% (see, e.g., page 340, column 2, top paragraph; page 341, column 1; page 342; page 344, column 1; page 344, column 2, bottom two paragraphs; page 345, Figure 4; page 346, column 1, top three paragraphs).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ek et al (U.S. 6,169,226 filed 29 May 1998) taken with Visser et al and Safford et al, in view of Kossmann et al.

The claims are broadly drawn to potato plants transformed with an antisense GBSSI construct and an antisense BE construct, wherein said plants exhibit decreased GBSSI and decreased BE activities, and produce starch with at least 90% amylopectin and increased phosphate content.

Ek et al teach and claim an isolated nucleic acid molecule comprising the potato starch branching enzyme II gene, potato plants transformed therewith in antisense orientation, and methods for obtaining starch from said transformed plants, wherein modification of starch to

reduce amylose content and other properties is desirable for industrial applications (see, e.g., column 1, lines 18-43; column 5, lines 30-50; claims 1-2 and 14-24). Ek et al also suggest the transformation of plants with both a branching enzyme antisense construct and an antisense construct to a second gene such as GBSSI, and also suggest the use of the BEI gene (see, e.g., column 6, lines 9-19; claims 2-3).

Ek et al do not explicitly teach transformed potato plants containing both an antisense GBSSI construct and an antisense BEI construct, wherein said plants produce starch with increased phosphate content or other desirable properties.

Visser et al teach transformed potatoes containing an antisense GBSSI construct, as discussed above, wherein said potatoes exhibit decreased GBSSI activity and produced starch containing 100% amylopectin (see, e.g., page 289, Abstract; page 293, Tables 1-3).

Safford et al teach transformed potatoes containing an antisense BE construct, wherein said potatoes exhibited decreased branching enzyme activity, as discussed above, and also teach that the plants produced a starch with modified structural properties and increased phosphate content (see, e.g., page 155, Abstract; page 158, column 2, bottom two paragraphs and Table 1; page 159; page 163, Figures 5 and 6).

Kossmann et al teach the desirability of genetically modifying potato plants to produce starches with 100% amylopectin and increased phosphate content for industrial applications (see, e.g., page 30, top two paragraphs; page 31, second through fourth paragraphs; page 34, first full paragraph and bottom paragraph; page 37, fifth and seventh full paragraphs).

It would have been obvious to one of ordinary skill in the art to transform potato with an antisense branching enzyme construct as taught by Ek et al, and to modify that process by incorporating the GBSSI antisense construct taught by Visser et al and the BEI antisense construct taught by Safford et al, in order to obtain 100% amylopectin starch with increased phosphate content for industrial applications, as suggested by Ek et al and Kossmann et al.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May 17, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638